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Science News x

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MUSCULAR ACTIVITY AND CARBOHYDRATE METABOLISM[1]

THE PROBLEM: INTRODUCTION

IT has long been discussed whether the breakdown of carbohydrate, rather than of other substances, is primarily responsible for the provision of energy in muscular contraction. It is known and accepted that work may be done, in the general melting-pot of the body, by the use of any kind of foodstuff. We are now concerned, however, specifically with the *primary* process of muscular contraction. In the complete chain of processes involved in long-continued exercise, this primary process may be disguised, or even apparently obliterated, by simultaneous transformations which take place between the different food constituents. Considering the internal combustion engine, it is obvious that petrol and benzole may be used indiscriminately for providing power and driving the machinery. In the same way, however, as we ask whether carbohydrate is the specific fuel of muscle, or whether fat may be used in an identical manner, so we might query whether petrol or coal can be used in an internal combustion engine. The obvious answer is that coal must be prepared beforehand by distillation, before it can be used in the engine, while petrol can be used directly; and that in the preparation of coal to form benzole for use in the engine, a considerable proportion of the energy of the coal is wasted, as regards its work-producing power. Putting our problem in terms of the modern theory of muscular activity and assuming that the initial process in contraction—that which causes the mechanical response—is an entirely non-oxidative one consisting of the formation of lactic acid from glycogen, we are asking now whether the recovery process by which the lactic acid is restored to its precursor can go on at the expense of *any* oxidation, or *only* of that of carbohydrate. *May the recovery mechanism, so to speak, be driven by any kind of combustion, as a steam engine may be, or is it necessary specifically to combust carbohydrate?*

THE RESPIRATORY QUOTIENT

It has long been known that the respiratory quotient during prolonged steady exercise is not unity. It varies with the diet. That, however, does not an-

[1] A lecture delivered at the request of the Mayo Foundation, at Rochester, Minnesota, and at the Universities of Iowa, Nebraska, Minnesota, Wisconsin and Michigan, in October and November, 1924.

swer our question. Carbohydrate may be used exclusively in the muscular process of breakdown and recovery, but as fast, or almost as fast, as it is used up it may be restored, in the general metabolism of the body, by the breakdown of some other substance, *e.g.*, of fat. The combustion of carbohydrate, followed by the reformation of carbohydrate from fat, would affect the respiratory quotient in a manner exactly similar to the direct combustion of fat.

Mechanical Efficiency on Different Diets

The beautiful and very convincing experiments of Krogh and Lindhard (1), published in 1920, showed with little possibility of doubt that the combustion of carbohydrate has some special connection with muscular activity. Employing a method where the respiratory quotient may be determined with an average error of only $\pm$ 0.002, measuring the cost of doing a given amount of work of moderate intensity in a highly trained and carefully observed and calibrated subject, and varying the substances metabolized by varying the diet during and before the experiment, they found the cost of work (*i.e.*, the total amount of energy used in doing a given amount of work) to be a linear function of the respiratory quotient, falling as the respiratory quotient rose. Of the total energy used in any effort, granting that the respiratory quotient be correctly measured, the fraction which is derived from fat may be shown to be a linear function of the respiratory quotient. I say intentionally, "*if the respiratory quotient be correctly measured*": we will discuss later the variations of respiratory quotient produced by lactic acid in the body, during and after severe muscular work. Such variations, however, do not affect Krogh and Lindhard's experiments, where the exercise was moderate, requiring only about one liter of oxygen per minute, and continued for a long time. If now we assume that carbohydrate oxidized is utilized directly for work, or (more accurately) for recovery from work, and fat only after "conversion" involving metabolic processes and loss of energy, the cost of work should be a linear function of the respiratory quotient—as Krogh and Lindhard found. As the mean of a long, careful and carefully weighted series of observations, which give one all the impression of extreme reliability, they found, assuming carbohydrate to be utilized directly for the production of work (or, as I should rather say, for carrying on the recovery process) that fat may be so used only after "conversion" involving a 10 per cent. loss of energy: in modern terms, the recovery process is 10 per cent. less efficient when fat is oxidized than when carbohydrate is oxidized. This suggests strongly that the primary breakdown is of carbohydrate, and that fat is used only in a secondary manner, *e.g.*, to restore the carbohydrate which has disappeared. These experiments of Krogh and Lindhard are particularly valuable since they were made on intact animals, namely, healthy men, and involved the complete process in the whole mechanism.

Lactic Acid

The most important line of evidence in this connection starts from the work of Fletcher (2) and of Fletcher and Hopkins (3), leading to that of Meyerhof (6), Embden (4), (5), and others. The phenomena of muscular fatigue are known to all, both personally and in the laboratory, as also is the effect of oxygen thereon. An isolated muscle stimulated in nitrogen soon fatigues and never recovers: an isolated muscle stimulated in oxygen may go on contracting for days. These observations of Fletcher's led to the lactic acid story (3). In an isolated muscle at rest and without oxygen the acid accumulates slowly, faster at a higher temperature; with a sufficient supply of oxygen it remains at a low value. Stimulation also will produce lactic acid: in oxygen this lactic acid is removed. According to Embden and his coworkers, the origin of this lactic acid in the muscle is a hexose di-phosphoric ester. They succeeded in isolating an osazone similar to that described by Harden and Young in the case of yeast. This hexose phosphate is presumably a very unstable substance; it has not been isolated from muscle; its amount can be estimated only indirectly and on certain assumptions. Embden regards it as the immediate precursor of the lactic acid which appears, though Meyerhof's experiments make it clear that it is glycogen which bears a quantitative relation to lactic acid. The amount of Embden's "lactacidogen" present in a muscle at any moment must be estimated by measuring the inorganic P_2O_5 immediately after, and one or two hours after, the fine division of the muscle: the increase in the P_2O_5 is supposed to represent the "lactacidogen" which has broken down. The evidence, though indirect, appears to yield results so definite that it is difficult not to believe that hexose phosphate is somehow intimately concerned with muscular activity. After severe muscular work, following a dose of phloridzin in rabbits, and after strychnine convulsions in rabbits and in dogs, there is a marked diminution in the "lactacidogen" present in their muscles. It is interesting too to record that, according to a communication of Robison and Kaye to the British Biochemical Society, the injection of insulin causes an increase in the "lactacidogen" of muscle. It must be admitted, however, that the rôle of the hexose-phosphate is not yet clear.

THE CARBOHYDRATE ORIGIN OF LACTIC ACID

It is very natural to attribute a carbohydrate origin to the lactic acid which is concerned so intimately with muscular contraction. By the fermentation of various types of carbohydrate lactic acid may be formed, and Meyerhof (6) has shown by a series of direct experiments, confirmed by independent methods at Cambridge by Foster and Moyle (7) that when lactic acid appears in muscle, whether from anaerobic conditions or from fatigue, an equivalent amount of glycogen disappears; in the converse process of recovery when the lactic acid is removed, glycogen reappears, not this time in equivalent amount but with a 25 per cent. loss, which is accounted for by the oxygen used and the heat produced in the recovery process. In the isolated muscle, therefore, there can be no doubt that lactic acid has a carbohydrate origin and is restored to carbohydrate in recovery, a fraction of it only being used in the oxidative processes required to drive the recovery mechanism. That this recovery reversal of the glycogen-lactic acid breakdown is, at any rate in isolated muscle, carried out at the expense of energy derived from carbohydrate oxidation, is made the more certain by Meyerhof's observation that *the respiratory quotient of recovery is unity*. Moreover, in the isolated muscle there is no sign of any diminution in the fat contained in the muscle, as was shown by Winfield (8) and confirmed to some degree by later and more severe experiments at Manchester (unpublished). The total amount of glycogen present in a muscle is adequate to account for the whole of the energy used in the most prolonged series of contractions that that muscle is capable of carrying out in oxygen, even under the most favorable conditions (9). It is possible, of course, that no transformation or combustion of fat is possible without the cooperation of other organs (*e.g.*, the liver) or of the body as a whole. We shall see later how far this objection applies. In the isolated muscle, however, we may safely assert that the only processes which are known to occur, the formation of lactic acid from glycogen in the initial phase and the removal of the lactic acid, coupled with the oxidation of a small amount of it in the recovery phase, involve nothing but reactions with, and by, carbohydrate.

PANCREATIC CONTROL

Azuma and Hartree (10) have shown that insulin has no effect whatever on the recovery oxidation in isolated muscle, and Foster and Woodrow (11) that it has no effect on the lactic acid formation in resting surviving muscles. In intact animals under insulin treatment glycogen tends to disappear from the muscles (Dudley and Marrian (12)) possibly partly to form a hexose phosphate, certainly not to form lactic acid. Moreover, Himwich, Loebel and Barr (13) have found that lactic acid formation in the diabetic individual is just as much the basis of muscular contraction as in the normal. This has been confirmed independently by my colleagues Long, Lupton and Hetzel (hitherto unpublished), not only in the case of the formation of lactic acid but in that of its removal in recovery. Apparently lactic acid is just as much involved in the mechanism of contraction in the diabetic as in the normal man. That there is, however, some factor in the pancreas concerned in the carbohydrate metabolism of muscle was shown by preliminary observations of Hopkins and Winfield (14) in 1915, who found that pancreas preparations have an inhibitory action on the formation of lactic acid in minced muscle. Apparently in the pancreas there is a substance, stable at high temperatures, which has a controlling action on the carbohydrate breakdown of muscle. This substance is not a ferment, and may be present in commercial pancreas preparations several years old. Foster and Woodrow (11) followed up this clue and established the fact that there is an inhibitory agent for the anaerobic lactic acid formation in muscle, which may be isolated from the pancreas and produces considerable inhibition even under conditions leading usually to the maximum lactic acid formation. This substance is not insulin, which has no such effect. They suggest that this new unknown substance has a specific controlling function on the carbohydrate metabolism of muscle, and that carbohydrate metabolism may be grouped into two great subdivisions, that of the body as a whole under the control of insulin, and that of muscle, to some degree under the control of this new pancreatic hormone.

ANALOGOUS METABOLISM IN OTHER CELLS

An interesting side-line from Foster and Woodrow's experiments arises when we remember that, according to the modern view of muscle, the basal metabolism of the intact animal is in large part the recovery from the resting lactic acid production of its muscles. This new pancreatic hormone might be expected, therefore, to control the basal metabolism, and possibly we may find in it a means of antagonizing an over-activity of the thyroid—though that is guesswork. Foster and Woodrow, on the basis of these experiments, have put forward the theory of carbohydrate metabolism (just referred to) to which, on quite other grounds, those who have been working on muscular activity have been inevitably reduced, namely, that the carbohydrate metabolism of muscle is a different thing from that of the body as a whole. That this carbohydrate metabolism of muscle, how-

ever, involving lactic acid, is not unique is indicated by many lines of evidence. For example, Stephenson and Whetham (15) have found that *Bacillus Coli*, in a medium containing glucose, uses oxygen if it can get any, and produces CO_2 and lactic acid: in nitrogen, CO_2 and lactic acid are produced up to a certain limit, the fermentation being a self-inhibited one: in oxygen less lactic acid is produced, more CO_2 is liberated and more oxygen is used. Apparently these organisms, in the presence of sufficient oxygen, can break down glucose completely to CO_2 and water. In the absence of sufficient oxygen they break it down, as does muscle, to lactic acid. If suspended in a medium containing no glucose but ammonium lactate, in the absence of oxygen they can do nothing; in the presence of oxygen they can produce CO_2 and use up oxygen, as does a muscle carrying out its recovery process.

Again, Warburg (16), using the delicate gas-manometer method of Barcroft, has measured the CO_2 produced and the oxygen used by various tissues suspended in a glucose-Ringer solution. Some of the CO_2 is produced by combustion of carbohydrate, some is driven out from preformed bicarbonate by acid formation. Expressing as "extra CO_2" the amount of CO_2 produced in excess of that derived from the oxygen used in burning carbohydrate, the "extra CO_2" is a measure of the lactic acid produced by the fermentation of glucose, that is, of the carbohydrate broken down, while the oxygen used is a measure of the carbohydrate oxidized. Normal tissues give a ratio, (extra CO_2)/O_2 of practically zero. Cancerous tissues from a rat, however, give an average ratio of 3.6: human cancerous tissues give a ratio usually from 2 to 4, but varying over wide limits. In normal tissues, therefore, the oxidative process of glucose metabolism is effective and the fermentative process is small: in cancerous tissues the oxidative process is ineffective and the fermentative process is large. If Warburg is correct, the cancerous tissue *is like a muscle in which the recovery mechanism has almost broken down.*

Glyoxalase

In all tissues of the body except the pancreas Dakin and Dudley (17) found a ferment, glyoxalase, which is capable of transforming methyl glyoxyl $CH_3.CO.CHO$ into lactic acid $CH_3.CHOH.COOH$. This ferment is inhibited by excessive acidity, that is, by an accumulation of the product of its own activity. It is present also in the blood of diabetic persons and in the blood and liver of diabetic dogs. An extract of the pancreas inhibits this reaction, and Dakin and Dudley have called this inhibiting substance *antiglyoxalase*. Antiglyoxalase is destroyed by heat, and on other grounds also it would appear not to be the same as the pancreatic hormone of Hopkins and Winfield, and of Foster and Woodrow. It is conceivable that the normal path of carbohydrate metabolism may lie through the formation of lactic acid by glyoxalase from methyl glyoxal; unfortunately, except for the presence of this potent enzyme glyoxalase, there is little evidence, either for or against this theory.

The Fate of Lactic Acid in Recovery

The fate of lactic acid, which is an undoubted intermediary in the breakdown of carbohydrate in the muscle, was long debated. Its removal during recovery, as established by Fletcher and Hopkins, was naturally credited at first to a simple process of oxidation. There were, however, certain fundamental difficulties about this to which there seemed to be no answer. The heat of combustion of glycogen, from which it is formed, is, according to Slater (18), 3,836 calories per gram, when the glycogen is in its fully hydrated form, as it occurs in solution in the muscle: that of dissolved lactic acid is 3,601 calories (Meyerhof), leaving a total energy for the transformation of the one to the other of only 235 calories. This small quantity then is the total energy available in the initial transformation of glycogen to lactic acid, while in the complete process, if the lactic acid were then oxidized, 3,836 calories would be liberated. The mechanical efficiency, therefore, of muscular contraction, supposing *the whole* of the initial energy were turned into work, could not exceed 6 per cent. Values of 25 per cent. have been found in the case of man. Actually the initial liberation of heat[2] per gram of lactic acid formed in muscle is larger than 235 calories, being about 296 calories. The difference has been attributed by Meyerhof to the neutralization of the acid by buffered alkaline protein salts inside the muscle fiber. There is no doubt that the acid is neutralized as soon as it is formed, since the hydrogen ion concentration does not rise appreciably. Moreover, there is not enough phosphate or bicarbonate present in the muscle to neutralize all the lactic acid formed. Neutralization by phosphate and bicarbonate liberates only a little heat, while that by buffered protein salts liberates a large amount. Even assuming, however, that 296 calories are liberated in the initial phase and that the whole of this energy is turned into work, if the lactic acid were then oxidized the efficiency could still be only 8 per cent. Clearly the lactic acid is not oxidized.

It has proved possible, moreover, to measure the total amount of heat liberated in the recovery process

[2] Total anaerobic (370 cals.) less delayed anaerobic heat (74 cals.)

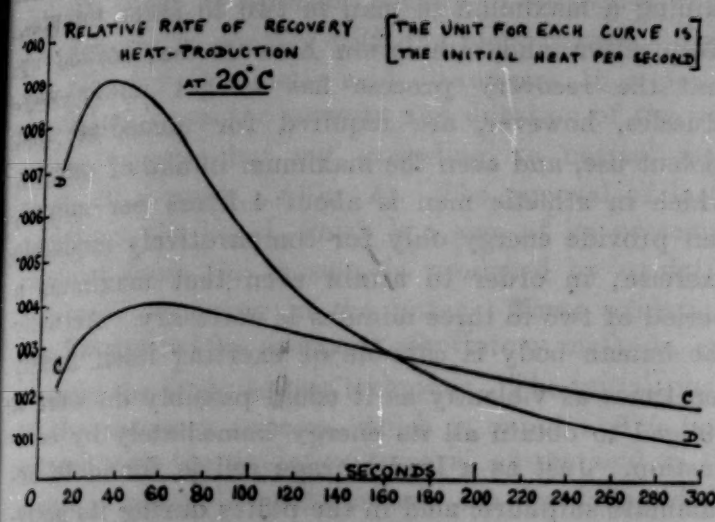

FIG. 1. Delayed heat-production of an isolated muscle in the presence of oxygen: C .03 sec. and D .20 sec. tetanus. (Hartree and Hill, 1922.)

(fig. 1), which in the latest and most careful measurements has come out almost exactly equal to the total heat liberated in the anaerobic phase. Thus, in the formation and the subsequent removal of a gram of lactic acid only 740 calories of heat are found, which is only about one fifth of what would occur if the lactic acid once formed from glycogen were subsequently oxidized *in toto*. Apparently of every 5 molecules of lactic acid removed in the recovery process only one is oxidized; the remaining four are restored to the place, or as the substance, from which they arose. There is no possibility of any error in the general conclusion to be drawn from these heat measurements: the difference to be explained is far too large; probably indeed the heat measurements provide us with the most accurate means of determining the "efficiency of recovery," as we may call it (or, in Meyerhof's term, the "oxidative quotient"), that is, the ratio of the amount of lactic acid removed to that oxidized in its removal. The best value to assume seems to be, in frog's muscle, about 5 to 1, and this is confirmed, as I shall show later, by two independent lines of experiment on man. This conception of the fate of lactic acid has been confirmed by Meyerhof's direct observations of the glycogen restored and the lactic acid lost during the recovery process. All lines of experiment, therefore, on the isolated muscle indicate about the same value for the efficiency of recovery. There is no doubt that one must regard lactic acid in muscle as being not so much the fuel as part of the machinery.

THE RECOVERY PROCESS

Consider now the recovery process in further detail. In the whole animal, without special precautions which we shall discuss later, it is not easy to isolate the recovery process from other events in the animal at large. In the isolated muscle the chemical method of investigation is not sufficiently analogous to what happens during normal existence, since the oxygen supply is cut off from its normal route by the cessation of the circulation, and (having to depend upon diffusion) is necessarily inadequate. *The oxidative removal of lactic acid in isolated muscle stimulated to severe fatigue has to take place under conditions of severe oxygen want, and is a very protracted affair.* The speeds, for example, at different temperatures can not be compared since they depend simply upon the rate at which oxygen can pass in, by diffusion from outside. Fortunately another method is available which, compared with the chemical method, is of surpassing sensitivity, namely, that in which the heat-production is measured (19). Myothermic technique is so sensitive, and so well under control, that it is possible to measure and to analyze the course of the heat production for many minutes after only a single twitch of the muscle, in which case the total amount of energy involved and the total amount of oxygen used are so small that the amount of the latter originally dissolved in the fluid of the muscle is more than adequate to account for the whole of the oxidation carried out. We are independent therefore of the oxygen supply, and can study the speed and magnitude of the recovery process in a muscle provided with an entirely adequate amount of oxygen.

We find, when we stimulate a muscle, that there is initially a large production of heat, which must be attributed to the formation of lactic acid from glycogen and its subsequent neutralization. Then commences a slow process of recovery, in which heat is liberated continuously for many minutes until the muscle has been completely restored to its initial condition. The heat production rises rapidly at first, attains its maximum in a few seconds to half a minute, and then slowly falls to zero again, along a curve which is roughly exponential. This curve of recovery heat production is the thermo-dynamic outline of the recovery process, into which fuller details must be drawn later by biochemical analysis. The speed of the process depends on temperature: it is increased very largely by a rise of temperature, decreased by a fall, so that in a frog at 0° C. complete recovery, even from a few hops, must take an hour or more! Extrapolating the results on frog's muscle to the temperature of the human body, the recovery process from moderate effort should be nearly complete in two to three minutes, given an adequate supply of oxygen: as indeed we find it to be. Its speed depends also on the size of the initial breakdown of which it is the result, not only absolutely

but relatively. Its speed is affected by the hydrogen ion concentration, being diminished by a rise and increased, up to a certain limit, by a fall, beyond which, however, it remains constant. Carbon dioxide, in concentrations of 10 to 15 per cent., produces a considerable fall in the rate of the recovery process, working much more quickly than do other acids, presumably because CO_2 can more easily penetrate the muscle fiber. The effect of hydrogen ion concentration on the speed of the recovery oxidation is analogous to that on the speed of autoxidation of glutathione or cystein. The total extra amount of heat liberated by oxidation in the recovery process is almost exactly equal to that set free in the anaerobic breakdown alone.

The "Accumulator Function" of Muscle

These facts have led us to the conception of the muscular machine as an accumulator of energy, analogous in its way to a lead electrical accumulator. The initial discharge, which may take place at a high rate, depends in no way on the oxygen supply: the final recharge, which is slower, depends directly on oxidation. In voluntary muscle all oxidation must be regarded as recovery oxidation: even though oxidation takes place during continuous exercise, and appears to be contemporary with the exercise, it must really be regarded as recovery from previous elements of the exercise.

It is probably not true to assert that in all organs and tissues oxidation is recovery oxidation. For example, Starling and Verney have recently shown that in a kidney secreting normally the administration of KCN, which abolishes oxidation, produces immediately a change in the secretion, making it in all respects similar to a filtrate from the blood. Apparently "knocking out" oxidation immediately "knocks out" the capacity of the tubule cells to perform their normal function. It is probable that the same immediate dependence upon oxidation exists in other tissues. Possibly those organs, in which sudden and violent activity may be required at a moment's notice and which are stimulated to activity through nerves, tend to act, as does voluntary muscle, like an accumulator: while slower tissues, in which rapid and violent response is not so necessary, may be content to remain dependent for their energy on oxidation, as does an internal combustion engine.

The Recovery Process in Man

The conception that all muscular oxidation is really recovery oxidation has produced an extensive change in outlook in regard to respiratory experiments on man. One of the fundamental difficulties of a large animal is the supply of oxygen to his tissues. When muscular exercise starts the oxygen intake rises, attaining a maximum in man in two to three minutes. Respiration and circulation have to be worked up and the recovery process has to get under way. Muscles, however, are required for immediate and violent use, and even the maximum intake of oxygen, which in athletic men is about 4 liters per minute, can provide energy only for comparatively moderate exercise; in order to attain even that maximum a period of two to three minutes is necessary. Actually the human body is capable of exerting itself nearly ten times as violently as it could possibly do were it obliged to obtain all its energy immediately by combustion. Just as a lead storage cell is found to accumulate sulphuric acid in the plates during its activity, so a muscle is found to accumulate lactic acid: just as the storage cell has its sulphuric acid removed from plates to solution during recharging, so the muscle has its lactic acid restored to its precursor in recovery. With this conception it is of interest to study the process of recovery not only in isolated muscles but in man, and in the last few years this study has proceeded a considerable way, especially by the efforts of my colleagues Long and Lupton. Lupton, alas, has not lived to reap the reward of his devoted work, or to realize the full importance of what he did.

Lactic Acid in Man

Lactic acid may be studied directly in man by its estimation in blood removed in the usual way from a vein. During muscular activity the lactic acid in the blood rises, attaining finally, if the exercise be continued long enough, a maximum characteristic

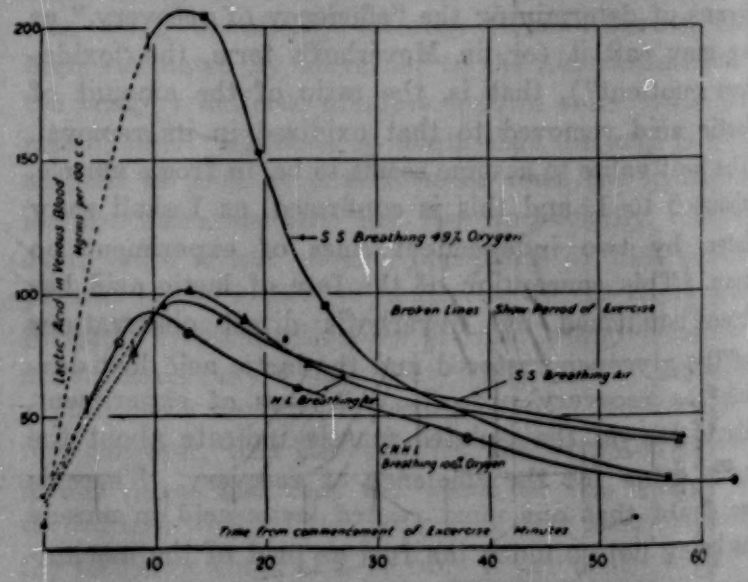

Fig. 2. Lactic acid in human blood after severe muscular exercise; two experiments in air, one in 49 per cent. oxygen, one in 100 per cent. oxygen. Note that the recovery process is not quite complete at the end of the time shown in the diagram. (Hill, Long and Lupton, 1924.)

of the effort made. After awhile the lactic acid distributes itself by diffusion equally in all tissues which are directly in contact with the blood stream. During recovery this lactic acid disappears, in a period depending upon the severity and duration of the preceding exercise but not exceeding, in normal man, about 90 minutes. (Fig. 2). The removal of lactic acid from the blood, which is a sign of its preceding removal from the muscle, is produced by oxidative processes occurring in the latter. These oxidations can be studied by ordinary respiratory methods, employing the Douglas bag technique. The initial phase of the recovery process, which is rapid and is concerned with the oxidative removal of the acid in the muscles where it was formed, can be followed by means of collections in a series of bags. The recovery oxidation falls rapidly, and after moderate exercise reaches zero in a few minutes. If, however, the exercise was severe, the lactic acid will have had time to escape from the muscles into the blood, and into other tissues in contact with the blood, and a second phase of recovery will occur, the removal of lactic acid which has escaped. This second phase may be very protracted and last as long as 80 minutes. The total oxygen used in the recovery process in this way we have named (20) the *"oxygen debt at the end of exercise."* Assuming, what may be shown to be very nearly true, that it is all used in the oxidative removal of lactic acid, and employing a value of 5.2 to 1 for the efficiency of recovery, we may calculate from the oxygen debt the lactic acid present in the body at the end of exercise. We find that *3 grams* or more of lactic acid may be liberated *per second* in the muscles of a powerful man, and that the body is able to tolerate an amount up to a *total of 130 grams.* The oxygen debt may attain a value of 18.7 liters!

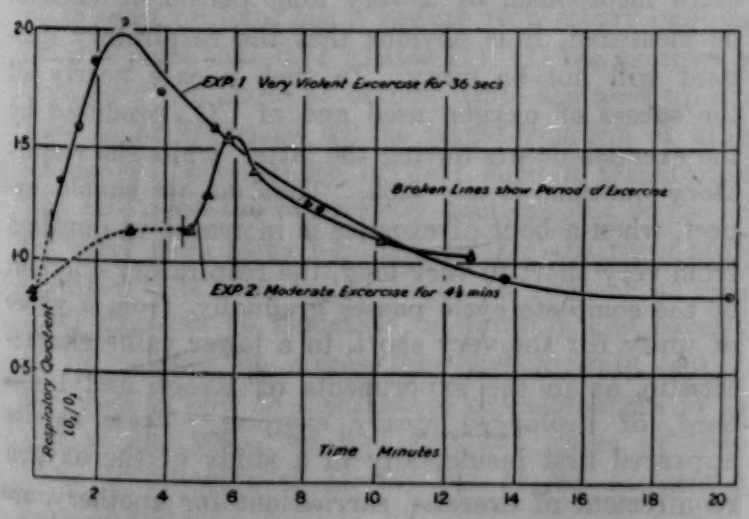

FIG. 3. The respiratory quotient during and after muscular exercise. These figures show the initial phase of recovery only. The final phase is shown in fig 4. (Hill, Long and Lupton, 1924.)

This lactic acid formation, therefore, in the human body is not a small or unimportant factor in muscular exercise; it is the keystone of the whole structure and has a large, indeed a preponderant, effect on the respiratory quotient (21). The respiratory quotient varies in a striking manner, up and down, during the onset of severe exercise and in recovery from it. At first it rises (fig. 3), attaining a value up to 2, during and immediately after the phase of lactic acid liberation, and while the respiratory center is still endeavoring to cope with the increased hydrogen ion concentration of the tissues. Before the hydrogen ion concentration of the body can have returned to its previous resting value an amount of CO_2 must be driven off equivalent to the lactic acid still present. After this previous level of the hydrogen ion concentration has been attained, which happens several minutes after recovery has commenced, the lactic acid continues to decrease and CO_2 has to be retained by the body, since otherwise the latter would become far more alkaline than previously. In the later stages of recovery the CO_2 retained is a measure of the lactic acid removed and very low values of the respiratory quotient may be found, down to 0.6 (fig. 4). Assuming this CO_2 retention to be a measure of the lactic acid removed, and the oxidation in excess of the basal value a measure of the lactic acid oxidized, we may determine in man the efficiency of recovery by respiratory methods, and its value comes to about 5 to 1, the same as in isolated muscle. Another method may be used in estimating the same quantity in man. If the lactic acid found in blood be assumed, in the later stages of recovery, to be uniformly distributed in all the soft tissues of the body which are in immediate contact with the blood stream, we

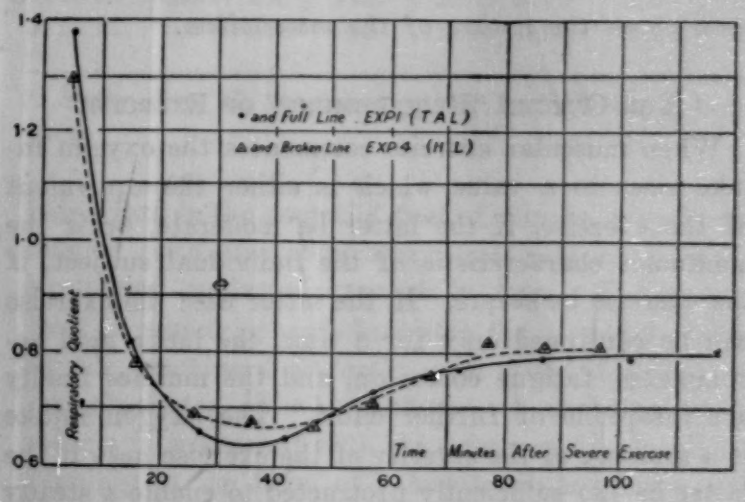

FIG. 4. The respiratory quotient after severe muscular exercise. Note that in the later phases, while carbon dioxide is being retained to compensate for that initially driven off, the respiratory quotient falls to a very low level, returning to its final value at about 80 minutes. (Hill, Long and Lupton, 1924.)

may calculate by two observations of the blood over any interval the total amount of lactic acid removed, and from the excess oxygen used in that interval we may again determine the ratio of lactic acid removed to lactic acid oxidized. We find as before a value of about 5 to 1, so that in the complete and intact animal the mechanism of recovery appears to be the same as in the simple isolated muscle.

THE USE OF THE RESPIRATORY QUOTIENT

These large variations in the respiratory quotient, during severe exercise and in recovery therefrom, show how necessary it is to exercise the greatest possible precautions if we wish to draw any conclusions from the respiratory quotient as to the substance being oxidized. Such precautions were taken in the experiments of Krogh and Lindhard. The exercise must be moderate and very long continued, and the whole condition of the subject, particularly the hydrogen ion concentration of his tissues, must be "steady." Then only are deductions reliable: *otherwise the value of the respiratory quotient tells us more about the fluctuations of lactic acid in the body than about the nature of the metabolism.*

THE OXYGEN "REQUIREMENT" OF EXERCISE

When muscular exercise commences the oxygen intake rises to a value which is either the equivalent of the exercise, if the latter be moderate, or is the maximum characteristic of the individual subject, if the exercise be severe. In the latter case the exercise can be continued only for a time, the lactic acid accumulates, fatigue comes on, and the muscles finally are incapable of further effort. The oxygen intake is a measure of the severity of the exercise *only* if the latter be (a) sufficiently protracted to enable a steady state to be attained and (b) sufficiently gentle to ensure that there is not a constant accumulation of acid leading to an oxygen debt. Hence by a study of the oxygen intake and the CO_2 output we can never really determine the nature of the primary oxidations of muscular activity, since the exertion must be continued for a long time until the body and all its processes are in a steady state, and the primary reactions of muscular recovery may then be masked by other and secondary effects. The oxidation of carbohydrate required to drive the recovery process may be confused for example with a reformation of carbohydrate from fat.

This fact and others have led us to a study of what we call the "oxygen requirement." The subject of the experiment takes exercise of any character and of any duration, the total organ used during the exercise and in complete recovery from it being measured. An initial and a final estimate of the resting oxygen consumption give us a base line from which the total oxygen consumption resulting from the exercise, during and in recovery from it, may be calculated. The measurement of the oxygen requirement is valuable, since it can be made in the case of any type of exercise, *e.g.*, walking up a single flight of stairs, or in very violent exercise which could not be continued long enough to make a measurement of the oxygen intake possible or useful. It may be a valuable criterion of the mechanical efficiency of work, etc. The oxygen requirement for a short element of exercise is always a measure of the total amount of energy required by the body for that exercise, assuming, as we shall see below, the energy value for oxygen corresponding to the oxidation of carbohydrate.

THE R. Q. OF EXERCISE AND RECOVERY

Much greater interest attaches to the respiratory quotient when we consider, not only exercise, but subsequent recovery. Taking the case of a small element of muscular exercise, such as running slowly for 30 seconds, the resting respiratory exchanges are measured carefully, both before the exercise and after complete recovery. The expired gases are collected both throughout the exercise, and during a recovery interval sufficiently long to ensure that the metabolism has returned absolutely to its initial state. The *excess* oxygen used as a result of the exercise and the *excess* CO_2 given out are then determined by analysis and calculation: *they are found to be precisely equal.* The same is true of fairly violent exercise for a short interval. In the case, however, of very violent exercise, the recovery process may be very protracted and the respiratory quotient of the excess metabolism may be less than unity. If the extra metabolism of a very long period of exercise be measured, it is obvious that the respiratory quotient will not be unity. In such a case nearly all the excess of oxygen used and of CO_2 produced by the exercise occurs during the latter, while the respiratory quotient is say 0.85. Thus, as we should expect, when a bout of exercise is increased in duration from very short to very long, the respiratory quotient of the complete cycle passes gradually, from a value of unity for the very short, to a lower value characteristic, as in the experiments of Krogh and Lindhard, of prolonged steady exercise. These results appeared first incidentally in a study of the oxygen requirement of exercise, carried out for another purpose. We noted, however, that of about twenty experiments practically all gave a respiratory quotient of the excess metabolism of about unity, the mean value being 1.03 (21). The small excess we attributed to the fact that in these experiments recovery was

not quite complete, and the small CO_2 retention of the last phase had not come within our observation. Since then my colleague Dr. Furusawa has examined the matter more carefully. His experiments (see Tables I and II) show that the respiratory quotient of the excess metabolism due to a *short element* of muscular exercise is unity. This is the case, even if the subject, having lived for several days on a diet of fat and protein, has a resting respiratory quotient of little more than 0.71 (Table II). If the exercise be prolonged the stores of carbohydrate are used up and have to be reformed by the transformation of other substances, presumably of fat; such a transformation acts upon the respiratory quotient just as though fat itself were being oxidized, so that the respiratory quotient falls. Given, however, an element of muscular exercise, so moderate in duration and severity as to produce no measurable carbohydrate lack in the muscles and no disturbance of metabolism in the rest of the body, we find that *the whole oxidative cycle of recovery is carried out at the expense of carbohydrate.*

This confirms and amplifies the experiments of Krogh and Lindhard with which we started this discussion, and makes clear how the experiments on the isolated muscle, with their indication that carbohydrate is the essential fuel of muscle, may be reconciled with the respiratory quotients obtaining in prolonged moderate exercise in man. *The primary fuel of muscle is carbohydrate: the essential element in the machinery is lactic acid, itself derived from carbohydrate.* The breakdown of carbohydrate in muscle is associated with the presence of phosphates, possibly in the form of a hexose diphosphoric ester. What the further details of the process are we do not know, but it is difficult not to believe that the utilization of fat by muscles can occur only after its previous "conversion" somewhere in the body. Even a subject suffering from severe carbohydrate want (Table II) will oxidize carbohydrate, and carbohydrate alone, in the complete cycle of reactions resulting from an "element" of muscular exercise.

A. V. HILL

TABLE I.—(*Unpublished experiments by K. Furusawa*)

NORMAL DIET

R. Q. of Excess Metabolism Due to Exercise

Duration or Exercise Mins.	Steps per Min.	Duration of Collection Mins.	Excess Metabolism CO_2/O_2	R. Q.
0.5	92	10	355/350	1.00
0.6	64	10	485/490	0.99
1.0	146	20	2120/2037	1.04
1.0	160	31	4185/4048	1.03
2.0	208	76	11230/10251	1.09
10	120	60	8720/8900	0.98
12	160	85	19860/18620	1.06
15	146	77	25670/25960	0.99
20	146	110	41310/42210	0.98
28	146	63	49520/52900	0.94
30	120	70	20225/20345	0.99
30	146	105	49420/56230	0.88

Not postabsorptive but several hours after a meal.

Average R. Q. resting = 0.85

Average R. Q. excess metabolism = 1.02

(Up to 30 liters O_2.)

TABLE II

(Unpublished experiments by K. Furusawa)

FAT DIET

(Bacon, Butter, Milk, Fat Chops)

R. Q. of Excess Metabolism due to Exercise

Subject	Duration of Exercise Mins.	Steps per Min.	Duration of Collection Mins.	Excess Metabolism CO_2/O_2	R. Q.	Compare R. Q. at Rest
K. F.	0.33	272	22	2733/2570	1.06	0.72
K. F.	1.0	146	20	2400/2260	1.06	0.71
K. F.	2.0	146	30	3020/2964	1.02	0.75
K. F.	4.0	146	43	10525/10822	0.97	0.78
K. F.	7.0	146	50	13730/15145	0.91	0.72
K. F.	9.0	146	100	18910/19940	0.95	0.76
K. F.	9.0	146	88	18835/20420	0.92	0.77
J. L. P.	0.4	216	22	3260/3341	0.98	0.77
J. L. P.	0.5	196	25	2132/1966	1.08	0.77
J. L. P.	1.0	146	26	3300/3345	0.99	0.73
J. L. P.	1.0	162	24	5255/5256	1.00	0.75
J. L. P.	5.0	146	35	12910/13775	0.94	0.75

Fatty diet, K. F. five days, J. L. P. 3 days, before exps.

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GENERAL POLICIES OF THE CARNEGIE CORPORATION[1]

DURING the year comparatively little time has been required for the study of specific new enterprises, for the obvious reason that funds were not available to finance them. As a result, the trustees have been free to devote their energies primarily to the formulation for their own guidance of a tentative body of doctrine as to the general policies of the corporation, and more specifically to a consideration of the fields in which, for the present at least, it should concentrate its efforts. Some discussion of the principles underlying these policies may be of service in making more clearly understood the problem which faces the corporation with reference to any particular grant; for this problem is not a simple one, depending wholly, or even primarily, on the merits of that particular proposal, but a very complex one, involving a number of other factors which must also be taken into account before an intelligent decision can be reached. It should be said at the outset that certain of these factors have already been dealt with in the reports of the acting president for 1922 and 1923, and that the following paragraphs are to be regarded, therefore, as supplementary to the discussions in those reports, rather than as an attempt to cover even the most important elements in this many-sided problem.

[1] From the annual report of the president of the Carnegie Corporation of New York.

It may be of interest at this point to give some indication as to the number of those who in any one year have more than a theoretical interest in these questions. Apart from the projects brought up for consideration by the members of the board itself or presented on behalf of the boards of other Carnegie enterprises, the corporation acted last year on 397 applications. Of the cases in which a budget was submitted with the application, the amount asked for came to more than $40,000,000. In only 68 cases could any grant be made, and of these 33 were renewals of grants made in former years. It would serve no useful purpose to make public a list of the projects declined, but both the applicants and the public may be assured that one and all received consideration by the executive committee, and were brought by it to the official attention of the board, the action taken in each case being made parts of its records.

Turning now to the general questions of policy to which reference has been made, the corporation has given particular attention during the year to the following: the responsibility of educational foundations to the public and to public opinion; the relation between the diffusion of knowledge and the guidance of opinion; factors affecting the limitation of program; and relations with operating agencies.

PUBLIC OPINION

It is now generally recognized that there is no fundamental distinction between the responsibilities of universities supported primarily by public taxation and those of institutions supported primarily by private endowment—both are public institutions. It must also be recognized that educational endowments such as the Carnegie Corporation are essentially public and not private enterprises. Grants made by them are matters of public concern and, other things being equal, they should involve the largest possible degree of public participation in what is recognized on all sides to be a cooperative enterprise. It will not do for those in charge of such endowments to assume that so long as their own motives are completely disinterested, criticism as to their acts and policies should be limited to the wisdom of this or that particular grant. They must recognize that doubts as to the basic social utility of these organizations have long existed in the minds of men and women regarding whose sincerity there can be no question, whatever may be said as to the amount and accuracy of their information. While, for the moment at any rate, the extraordinary results which have been achieved through the grants of these bodies, particularly in the alleviation of human suffering, have operated strongly to increase public confidence,

no one can say whether this state of mind is to be permanent. The time may well come when the possibilities of usefulness open to the Carnegie Corporation, for example, will depend in large measure upon the number and distribution of those who can testify on the basis of actual experience that the organization does not regard itself as a dominating or patronizing force in carrying forward any particular program, but merely as one factor, and not the controlling factor, in cooperative enterprises for the advancement and diffusion of knowledge and understanding among the people of the United States. It is not enough for the trustees themselves to realize that the furnishing of funds, important as it is, is secondary to the knowledge and the labor of those who actually transform an idea into a reality; there should also be at least the nucleus of an understanding public opinion on the subject.

Diffusion of Knowledge and Direction of Opinion

While it would be exceedingly difficult and not particularly profitable to draw a hard and fast line between the diffusion of knowledge and the directing of opinion, it is clear on which side of the doubtful zone between the two the interest and the responsibility of the corporation should lie. The deliberate and conscious propagation of opinion is a perfectly legitimate function for the individual, but it is becoming generally recognized that it is not the wisest use to which trust funds can be put— and this entirely apart from the question whether, in any given case, those in charge of such funds may, as individuals, be sincerely and even enthusiastically in favor of the spread of the idea in question. Surely, the discovery and distribution of facts from which men and women may draw their own conclusions offers a field sufficiently wide and sufficiently vital to the welfare of humanity.

Limitation of Program

The foregoing are but two of many elements to be considered in determining the program of such a body as the Carnegie Corporation. Offhand, an income of six million dollars a year would appear to give freedom for practically an unlimited range of interest under the provision of its charter, but after all, six million dollars makes a very small proportion of one billion, and this latter is the sum which it has been estimated the United States requires or at any rate spends each year upon its philanthropies. The corporation must of necessity restrict its angle of vision and, at the best, it can support only a very small percentage of the projects which are brought to its attention, even from among those regarding whose usefulness to humanity there can be little question. Among the other factors to which consideration must in any case be given is that of the possibility of support from other sources. It would appear to be entirely proper for the trustees to recognize that certain undertakings can look with confidence to support for their general activities from what may be called a regular constituency. A well-established college or university, for example, may turn to its own alumni, and the members of a large and rich community served by some local institution like a library, or museum, or hospital, are more and more generally recognizing their direct responsibilities to such institutions. On the other hand there are enterprises, particularly in fields where experimentation and demonstration are still needed, which can not, certainly in the earlier stages of development, call upon any particular clientele. Many of these can not be undertaken at all unless appeal can successfully be made to the custodians of relatively unrestricted funds like those of the Carnegie Corporation.

There is another side to this question of the limitation of program which is not always borne in mind. When once a foundation has contributed to one or more typical enterprises in any given field, the others in the same field naturally turn to it for aid. Obviously, if it habitually contributes to a wide range of activities, its contribution in any single field must be correspondingly reduced, and those whose applications must of necessity be declined are often severely handicapped in securing funds from other sources, due to the impression that they have been tried and found wanting by the foundation in question. That this impression may be wholly unjustified does not undo the harm. In so far as the program of a foundation is recognized as being limited—not necessarily permanently, but for the time being at any rate—to certain definite fields within which all outstanding propositions can be considered on their merits, this unfortunate situation is less likely to develop.

In 1921, sixty-seven per cent. of the number of grants made and seventy-seven per cent. of the total sum voted, outside of the appropriations to other Carnegie enterprises, were in the nature of contributions to campaigns for the general endowment or equipment of institutions or for the general support of organizations. Since that year, the tendency on the part of the corporation has been more and more to support specific projects rather than to make such general contributions. As a result, the corresponding figures for the year now under review are as follows: forty-two per cent. of the number of grants and thirty-three per cent. of the sums voted.

While the application of this policy has naturally proved disappointing to organizations now engaged

in campaigns, it is believed that ultimately it will meet with general approval. The conditions facing the institutions of learning at the close of the war, together with good times, and the habit of generous national expenditure combined to create a series of endowment and building campaigns that swept like an epidemic across the country. A similar process developed in the interest of various associations and leagues and other similar groupings, many of which came into being at about the same period. Without prejudice to the good results obtained in many instances, it must be recognized that such a system of campaigns has its obvious disadvantages. In not a few cases, the campaigns were wastefully conducted, and in others sums received were not wisely spent. Too often the raising of funds for general expenses, and particularly for promotion expenses, becomes commercialized. This type of appeal presents an additional problem from the point of view of the foundations. In so far as these organizations are attempting to concentrate their efforts within certain recognized fields, and thus obtain from their grants cumulative results within those fields, contributions for general purposes, no matter how admirable in themselves, must be recognized as weakening their power to achieve these specific results. Fortunately, however, it is sometimes possible to make a contribution which serves to help the general financial situation of the institution in question and at the same time to carry forward, under particularly favorable circumstances, the development of an idea on which the corporation is, at the moment, concentrating its attention. A case in point is that of Harvard University, referred to on page 20. Within the means at its disposal, the corporation should always be ready to take advantage of such opportunities as they arise.

Operating Agencies

The Carnegie Corporation is not in itself an operating body. It certainly was not the intention of its founder that it should become so, and it does not seem probable that circumstances will arise which will make this step desirable. To determine the fields in which appropriations may most wisely be made and to select in general terms the special projects within those fields is in itself a sufficiently heavy responsibility for the trustees.

Later on in this report, on pages 13 and 14, some discussion will be found as to the relation of the corporation to other operating agencies. Naturally, however, its relations have been closest with those operating agencies which Mr. Carnegie had himself established, particularly the five of which the active head is, under the charter of the corporation, ex-officio a member of its own board. As an evidence of the closeness of this relationship, it may be pointed out that, since its organization, in all more than $43,000,000 has been voted by the corporation to these institutions in response to requests from them. These grants have been entirely within the purposes of the corporation as conceived by Mr. Carnegie, who had the foresight to realize that conditions might arise to render insufficient the endowments he had created for these other agencies, though their endowments at the time had seemed amply sufficient for their purposes. Since his death, to mention no other factor, the world-wide reduction in the purchasing power of money would have seriously crippled the work of at least four of these agencies if the corporation had not been in a position to come to their aid.

The Carnegie Corporation does not need money from these sister institutions, but in the solution of its own problems it does need help of other kinds, as in the carrying forward of enterprises which have been initiated by it. Something has already been accomplished along these lines, as the records of annual grants will show, but the trustees might profitably consider a rather searching study as to whether the corporation has taken full advantage of the peculiar relationship to its sister institutions which it enjoys.

Other Problems

The above by no means exhausts the list of problems of policy, really fundamental in their nature, which must be grappled with, and there is no doubt that the two succeeding years of the period of limited resources may be devoted to study with even greater profit than the year just closed. As a single example of the questions which face bodies like the Carnegie Corporation may be taken the question of the temporary annual grant. It is often a real privilege to provide the funds which enable some enterprise of public importance to make not only an appeal but a demonstration to the public which should ultimately support it. But it is rarely, if ever, that the corporation and the beneficiaries find themselves in agreement as to when this "temporary" aid should stop. The latter are persuaded with perfect sincerity that the amount involved, while a matter of life and death to them, is negligible to the corporation. It is not realized that in the aggregate these small sums, like the slender threads by which the Lilliputians bound Gulliver to the ground, become a very serious matter. Nor is it likely to be remembered that the corporation has always before it for consideration other commendable projects which can not be launched without just such help as they themselves have enjoyed.

CONDITIONAL GRANTS

Another problem to which intensive study could profitably be given is the conditional grant. It has its obvious advantages. A relatively small sum so offered will sometimes serve as a primer to produce an explosion of generosity from other sources. On the other hand, when the conditions have to do with certain specified methods of carrying out the project, we enter on debatable ground. The ideas behind the stipulations may in themselves be admirable, but should they not, if made at all, be suggestions rather than stipulations? It may also be questioned whether in some instances a conditional offer does not put too powerful a weapon in the hands of persons perhaps not fully qualified to exercise the responsibility of using it. It would not be difficult to cite instances in which local communities, or alumni, or religious bodies, have been dragooned by the use of this weapon into making contributions beyond their means and beyond the real needs of the institution in question.

RESEARCH

The opportunities open to the corporation in the field of research have been the subject of particular study for several years, but this is a topic which is not—and never will be—exhausted. During the present year, for example, it has been pointed out to the corporation that there are really two stages in most research processes, and that they are not necessarily best carried out by the same individual or the same agency. Breaking the trail is one matter, and broadening that trail into a road is another. The latter process is largely a matter of presentation and dissemination, but none the less it contains, or at any rate it should contain, an important element in research. A study of this whole question may prove to be of especial interest to the corporation.

FREDERICK P. KEPPEL

WILLIAM HENRY EMERSON

WILLIAM HENRY EMERSON was born at Tunnel Hill, Georgia, in June, 1860. He graduated from the United States Naval Academy in 1880. Was Midshipman from 1880 to 1882 and Ensign 1882 to 1884. He then resigned from the navy to pursue special studies at the Johns Hopkins University, from which institution he received the degree of Ph.D. in 1886, having specialized in chemistry. In the same year he accepted the appointment to the professorship of chemistry at the South Carolina Military Academy, Charleston, S. C., which position he resigned in 1888 to become professor of chemistry at the Georgia School of Technology, just then in process of organization. Here he remained until the day of his death, November 13, 1924, a period of thirty-six years. During this time he saw the institution grow from the experimental stage into one of the leading engineering and technical schools of the country. To him especially is due credit for the maintenance of high standards of scholarship, which have characterized the work of Georgia Tech. By temperament and training he was especially equipped to do research work on problems in his chosen field, and longed to do so, but with characteristic spirit he sacrificed opportunity which those who knew him believe would have placed his name high in scientific achievement, in order to carry on the heavy duties devolving upon the head of a department of a growing institution, and the additional great responsibility of the deanship, which he assumed in 1910.

Dean Emerson was awarded the degree of Sc.D. by the University of Georgia in 1912. He was a member of the American Chemical Society, Society for the Promotion of Engineering Education, Phi Kappa Phi (honor society), Georgia Academy of Sciences and Alpha Tau Omega Fraternity.

He published papers covering investigations he had made in the oxidation of mesitylene, the composition of cotton seed oil and also upon the marbles, coal and corundum of Georgia.

Dean Emerson married in 1887, and is survived by two sons and his widow.

J. L. D.

NED HOLLISTER

NED HOLLISTER, superintendent of the National Zoological Park since October 1, 1916, and one of the foremost mammalogists of the world, died on November 3, following an operation.

Mr. Hollister was born at Delavan, Wisconsin, on November 26, 1876, where he received his education and began the study of zoology. From 1902 to 1909 he conducted zoological field work for the U. S. Geological Survey in Texas, New Mexico, Alaska, British Columbia, Washington, Oregon, California, Utah, Nevada, Louisiana and Arizona. In 1910 he began his connection with the Smithsonian Institution, being appointed assistant curator of mammals in the U. S. National Museum, which position he held until 1916 when he was selected for the responsible position of superintendent of the National Zoological Park, Smithsonian Institution.

In 1911 Mr. Hollister was a member of the Canadian Alpine Club Expedition to explore the Mt. Robson region of British Columbia and Alberta, and in 1912 he represented the Smithsonian Institution on the Smithsonian-Harvard Expedition to the Altai Mountains, Siberia and Mongolia. The results of Mr. Hollister's scientific work have appeared in the pub-

lications of the Smithsonian Institution and in various technical journals for many years. Besides over 100 minor papers on zoological subjects, he was the author of a number of large works, including "The Birds of Wisconsin" (1903); "Mammals of the Philippine Islands" (1911); "Mammals of the Alpine Club Expedition to Mount Robson" (1913); "East African Mammals in the U. S. National Museum" (Vol. 1, 1918; Vol. 2, 1919; Vol. 3, 1923). This last is probably Mr. Hollister's greatest contribution to science, being a complete technical account of the great collection made in East Africa by Theodore Roosevelt, Paul Rainey and other collectors.

During Mr. Hollister's term of office as superintendent, the National Zoological Park underwent a steady growth and development. Many improvements to the grounds and animal quarters were carried out and he made every effort to provide for the enjoyment and convenience of the public. During the last few years, the collection of animals in the park has been greater in numbers and in scientific value than ever before, and the number of visitors to the park has increased steadily until it reached during the past year a total of 2,400,000. It was largely through Mr. Hollister's efforts that Congress was persuaded a few years ago to provide funds for the purchase of a frontage of 625 feet at the Connecticut Avenue entrance to the park, thus insuring for the future a dignified and appropriate approach.

Mr. Hollister was a fellow of the American Association for the Advancement of Science, a member of the American Ornithologists' Union, the Biological Society of Washington (president, 1921), Washington Academy of Sciences, American Society of Mammalogists (editor of the *Journal of Mammalogy*), honorary member of the Sociedad de Estudios Biologicos, Mexico, and a member of the Cosmos Club.

He is survived by his wife, Mrs. Mabel P. Hollister, and by his mother, two brothers and a sister.

X

SCIENTIFIC EVENTS

JACQUES LOEB[1]

By the death of Dr. Jacques Loeb the world has lost one of the great men of his generation; biology has lost one of the finest intellects that has ever been devoted to this branch of science; this laboratory has lost one of its most eminent members. He stood out among his fellows as an investigator, as a teacher and as a cultivated gentleman broadly interested in all aspects of nature and all the activities of men.

As an investigator he was tireless in energy, ingenious in experimentation and exceptionally gifted in insight. He lost little time on false leads, but rather blazed his trail straight into new territory and attained his objective by simple and crucial experiments.

He brought to his work a broad knowledge of related sciences. In the latest advances of chemistry and physics he was always informed, and his researches showed the breadth of his reading and the solid character of his scholarship. He had a poet's imagination held in check by practical and mathematical faculties of high order. Consequently his hypotheses were at once brilliant and founded on the best physico-chemical data available. He was ready to change his theories as new facts were discovered. He believed that explanations of phenomena must be expressible ultimately in mathematical terms. He profoundly influenced general physiology not only by his theories and experimental results but also, quite as much, by the emphasis he laid upon the quantitative method.

Professor Loeb came to Woods Hole first in 1892. The epoch-making discovery of artifical parthenogenesis was made at this laboratory. The antagonistic action of ions was demonstrated here. Many other researches which have influenced biological thought were carried on here and may be noted in the long list of papers and books which constitute his best monument. He founded the course in general physiology at Woods Hole in 1893 and directed it for several years. He was a trustee from 1897 to his death. From 1910 he directed the branch laboratory of the Rockefeller Institute in cooperation with the Marine Biological Laboratory.

As a teacher he was enthusiastic and inspiring. His lectures were in advance of the times and full of suggestions for research. With his graduate students he was helpful and friendly and at the same time critical and stimulating. Those who were his students know how enormously they profited by his inspiring personality.

As a man his interests were well-nigh universal. He found time to make himself familiar with a large literature. He enjoyed music and all the arts. He was interested in economics, sociology and government. His "Mechanistic Conception of Life" is an important contribution to philosophy and psychology.

He was a kindly man. He was a lovable man. He hated war and all sham. He had an incisive sense of humor and loved a harmless joke. He was the center of any company and he had many friends.

This is the man we have lost. Woods Hole is not the same without him, but the inspiration of his work remains in our midst.

To his family we extend our sympathy and on the pages of our records we inscribe this memorial.

[1] Minute adopted by the Trustees and Corporation of the Marine Biological Laboratory.

THE JAPANESE EARTHQUAKE OF SEPTEMBER 1, 1923

A PRELIMINARY report by Prof. A. Imamura, the first issued by the Imperial Earthquake Investigation Committee, has been published in the *Seismological Notes* of that committee and is abstracted in *The Geographical Journal*. Most of the instruments in the Seismological Institute at Tokyo were wrecked or dismantled by the first shock. Of the whole number, only one component of one seismograph registered the movement from beginning to end, an interval of two hours and twenty minutes, but within ten minutes from the first vibrations four seismographs were sufficiently repaired to continue their useful work, and others were added in the following days. Though few recorded more than the first tremors, these happened to be the most important, for, from the direction of the earliest vibrations and the duration of the preliminary tremors, the position of the epicenter was found to be in lat. 34° 58′·6 N., long. 139° 21′·8 E., or under Sagami Bay, and the depth of the focus to be roughly 15 kms. The survey of Sagami Bay, repeated by the Imperial Hydrographic Service, showed that an area of 700 sq. kms. had been depressed on an average by 39 fathoms, and another area of 240 sq. kms. raised on an average by 45½ fathoms. These movements naturally gave rise to sea-waves, which along the shores of Sagami Bay reached heights of 8, 9 and even 12 meters, and the remarkable feature of these waves was that the directions in which they advanced showed that the largest waves came from the areas of elevation, while those that came from the areas of subsidence were comparatively small. The great earthquake came without any warning fore-shocks, though four very slight shocks were registered at Tokyo during the preceding month, all of which had origins within or near Sagami Bay. The after-shocks, as usual, were very numerous, partly on account of the large focal area, partly because the first shock was followed in less than fifteen hours by another almost equally severe in a different part of the same seismic zone. During the first month, the total number recorded at Tokyo was 1,256, of which most of the strongest took place in the Sagami Bay area, though others originated within and to the southeast of the Bo-so peninsula, and also in a district to the north of Tokyo.

THE NEW SEISMIC STATION AT FORDHAM UNIVERSITY

THE new seismological observatory at Fordham University was dedicated on October 24. The building housing the seismographs is one of the few in the world devoted exclusively to this work, and the lately acquired "Milne-Shaw" seismograph installed there is the only one of its type possessed by any Jesuit observatory. It is the third of its kind, however, to be sent to this country. The building itself was erected by William J. Spain, of New York, in memory of his son, who was a student at the university, and died during his sophomore year.

The Milne-Shaw seismograph embraces practically all the advantages of the most sensitive type of apparatus, avoiding many mechanical complications, by reason of the method of direct photographic registration which it employs to reduce the motion of the earth to a graphic form.

It is this instrument that occupies the place of importance in the new building erected at Fordham for the study of earthquakes, although the edifice also contains other piers accommodating instruments of lesser sensitivity. Mr. F. W. Sohon, S.J., who was responsible for the detailed design of the interior, took into consideration the future development of the station and the large masonry pier on which the new seismograph stands is built to hold three instruments, two of the type already explained and a third known as the "Galitzin" vertical seismograph. When the station possesses these three machines not only the distance but the actual direction and specific location of the quake can be determined from this station, unaided by data from other sources. The reason for the three machines is the recording of the motion of the earth in three different directions, or rather the resolution of the motion of the earth into three components, one instrument recording the north and south horizontal motion, a second the east and west horizontal motion and the third the vertical motion of the earth.

The pier on which these instruments are to stand reaches to a depth of twenty-five feet, and is erected on bed rock; it is freed from local and artificial disturbances by a space between it and the floor of the building. The room in which it was erected is entered only by passing through an ante-room, from which visitors may view the installation through plate-glass windows. Beyond the instrument room proper is a photographic dark room and work shop for the development and interpretation of the records.

A special thermostat automatically controls the temperature of the building, keeping constant in all weathers, to within one degree. There is also a wireless installation in the building and the time signals received twice daily from Arlington are recorded directly on the seismograms, making the determination of the arrival of a quake accurate to less than one second. Communication by cablegram has been established with Professor Turner, of Oxford University, England, so that verification of data observed at both stations may be had in the shortest possible time.

PERMANENT PROGRAM OF THE CONFERENCE ON THE UTILIZATION OF FOREST PRODUCTS

THE first national conference on utilization of forest products concluded its sessions on November 21, after mapping out a permanent program and entrusting it to the central committee on lumber standards.

The program of activities as adopted calls for completion and general adoption and application of lumber standards, as recommended by the central committee; development of the application of better attention to the problems of piling, storing and drying lumber, in all its forms; wood preservation treatments; extension of use of decay prevention in pulp and pulpwood in storage; consideration of methods for arrest and prevention of decay in logs and lumber; encouragement of surveys with the object of utilizing waste products through diversified operations; development, improvement and unifying of buildings codes; improved designs of boxes and crates and other economies, and encouragement of improvements and economies by organized industrial units consuming forest products.

Lines of investigation which, in the opinion of the conference committee, require first consideration are: forest drain loss in the woods; sawmill waste and practices and machinery; best uses of so-called "inferior species"; properties of wood; a timber survey, embracing the supply, amount of land available by regions and classes of soil on which forests can now and later be grown, and the rate at which timber is now growing and the potential growing capacity of the land; wood-using industry survey; forest protection from fires, insects and tree blights, and possible use of tropical woods to supplement American high-grade hardwoods, being rapidly depleted.

The necessity of putting idle land to work in growing tree crops by the cooperation of the states with the federal government, through the medium of the Clarke-McNary Forestry Act, was pointed out.

SCIENTIFIC NOTES AND NEWS

IT is announced that the University of Paris will confer honorary degrees on seven foreigners, including Dr. Charles D. Walcott, president of the Smithsonian Institution and retiring president of the American Association for the Advancement of Science.

THE Holland Society of New York awarded on November 24 its gold medal for 1924 to Dr. L. O. Howard, chief of the Bureau of Entomology. This medal is awarded annually to an American for notable and distinctively American achievement in literature, art, science or public service.

DR. JOHN AUGUST ANDERSON, astronomer at the Mount Wilson Observatory, has been awarded the Howard N. Potts medal by the Franklin Institute of Philadelphia for his invention of a new form of seismograph and for his improvements in the ruling of diffraction gratings.

IN addition to the award of the Darwin Medal to Professor T. H. Morgan, announced in SCIENCE last week, the president and council of the Royal Society have made the following awards: Royal Medals to Sir Dugald Clerk, for his application of scientific principles to engineering problems, particularly to the development of the internal-combustion engine, and to Dr. H. H. Dale, for his researches in pharmacology and physiology; the Copley Medal to Sir E. Sharpey-Schafer, for his valuable work in physiology and histology; the Rumford Medal to Mr. C. V. Boys, for his invention of the gas calorimeter; the Davy Medal to Professor A. G. Perkin, for his researches on the structure of natural coloring matters.

WILLARD C. THOMPSON, professor of poultry husbandry at Rutgers University, and chief of the department of poultry husbandry at the New Jersey State Agricultural Experiment Station, has been appointed director of the National Poultry Institute of England.

DR. WILLIAM F. THOMPSON, director of the California State Fishery Laboratories, has been appointed director of investigation for the International Fisheries Commission provided under the Halibut Treaty between Canada and the United States. The commission has invited to act as a scientific advisory board Professor N. Cobb, University of Washington; Dr. C. McLean Frazier, chairman of the zoological department of the University of British Columbia, and Dr. A. T. Clements, of the Geological Station, Nanaimo, B. C.

DR. WILBUR A. SAWYER, assistant regional director in the east of the work of the International Health Board of the Rockefeller Foundation, has been appointed director of the public health laboratory service of the board.

DR. P. N. LEECH has been made director of the chemical laboratory of the Council on Pharmacy and Chemistry of the American Medical Association.

DR. E. P. CATHCART, professor of chemical physiology in the University of Glasgow, has been appointed a member of the Medical Research Council, England, in the place of Professor D. Noel Paton, who has retired.

DR. WM. S. JONES, PH.D. (Ohio State, '24), has joined the research laboratory of E. R. Squibb and Sons, New York.

D. H. CAMERON, of the division of physical chemistry of the Iowa State University, has resigned to accept a position with the Celite Products Company, of Los Angeles. His preliminary work will be to organize a research laboratory for the study of oil purification.

PROFESSOR A. E. VERRILL, from 1864 to 1907 professor of zoology in Yale University and since emeritus professor, sailed on October 29 for the Hawaiian Islands, where he plans to live and to continue his zoological work.

DR. THORVALD MADSEN, president of the Health Committee of the League of Nations and director of the State Serum Institute of Denmark, who has been making a six-weeks' study of public-health administration in the United States, sailed for France on November 26.

DR. CHARLES A. BAILEY, of the staff of the International Health Board, sailed on November 15 for Spain to assist the government health authorities in a survey of hookworm infection in the mines of the country.

RECENT visitors to the New York Botanical Garden include Dr. Hugo Glück, professor of taxonomic and pharmaceutical botany at the University of Heidelberg; Dr. Otto Stapf, for many years keeper of the Herbarium and Librarian of the Royal Botanic Gardens at Kew, England, and now editor of *Curtis's Botanical Magazine;* Professor C. H. Ostenfeld, director of the Copenhagen Botanical Garden, and Major T. F. Chipp, assistant director of the Royal Botanic Gardens, Kew.

G. G. SIMPSON, Othniel Charles Marsh research fellow in the Peabody Museum of Yale University, is undertaking a series of detailed studies of the Mesozoic mammals, based chiefly on that part of the Marsh Collection preserved in the Peabody Museum. It is hoped eventually to produce a monographic revision of these ancient and interesting small animals.

CAPTAIN ROBERT A. BARTLETT, Arctic explorer, who commanded the *Roosevelt* under Peary, announces that he hopes to start next spring on his three-year journey from Nome, Alaska, across the North Pole to Spitzbergen. In a boat of 400 tons, with a crew of ten men, and accompanied by two scientific men, Captain Bartlett hopes to realize his project, first announced two years ago, of drifting with the ice floes from the Bering Straits and across the Pole between Spitzbergen and Greenland on the northern coast of Norway.

COMMANDER BRUNS, German aviator, who in 1919 announced plans for a Zeppelin expedition to the North Pole, is visiting Christiania as the guest of Dr. Fridtjof Nansen, who is reported to have agreed to accompany him when he puts the plan into operation. The expedition will be a scientific one, and is not intended to compete with that of Roald Amundsen.

PROFESSOR P. DEBYE, professor of physics at the Technical Institute at Zurich and formerly professor at the University of Göttingen, will stay at the research laboratory of theoretical physics of the Massachusetts Institute of Technology, from January 5 to March 15, 1925. During this period he will give a series of lectures on "Some modern aspects of physical chemistry" and direct some research.

DR. V. H. BLACKMAN, professor of plant physiology and pathology at the Imperial College of Science and Technology of London and president of the botanical section of the British Association for the Advancement of Science, has been visiting and lecturing at several American botanical institutions. His first address was at the dedication of the Boyce-Thompson Institute for Plant Research at Yonkers, September 24, after which he lectured at the following universities and institutions: Columbia, Brooklyn Botanic Garden, Cornell, Michigan, Chicago, Wisconsin, Minnesota, Iowa State College, Missouri Botanical Garden, Bureau of Plant Industry of the U. S. Department of Agriculture and the Massachusetts Agricultural College. He was also guest of the botanical departments of Yale and Harvard and of some other institutions.

DR. WILLEM EINTHOVEN, professor of physiology at the University of Leyden, Holland, who was recently awarded the Nobel prize for medicine, gave a lecture to the combined Rush Society and Physiological Society of Philadelphia, on December 1, on the subject "The use of fine threads in physiology." On December 4, he gave the Newbold lecture at the College of Physicians on the "Relationship of the mechanical and electrical phenomena of muscular contractions with special reference to the cardiac muscle."

PROFESSOR E. FRANKLIN ARMSTRONG, president of the Society of Industrial Chemistry, London, addressed the scientific staff of the Rockefeller Institute for Medical Research on November 21, on: "The fats from many aspects."

DR. C. V. RAMAN, professor of physics of the University of Calcutta, now acting as research associate at the California Institute of Technology, addressed the members of the Southern California Section of the American Chemical Society at Los Angeles on November 7, his subject being "New light on atoms and molecules."

DR. I. M. KOLHOFF, conservator of the Pharmaceutical Laboratory, of the University of Utrecht, Holland, spoke before the Illinois section of the

American Chemical Society on October 13, on "Potentiometric titration."

PROFESSOR WILLIAM MORRIS DAVIS delivered a series of four lectures from November 12 to 18 before the students of geography and geology at Southern Methodist University, Texas, entitled, "Scientific methods of study," "Modern geography," "The Lesser Antilles" and "The Grand Canyon of Arizona."

DR. S. C. LIND, the chief chemist of the Bureau of Mines, delivered an address on "Helium and its uses" before the Brooklyn Institute of Arts and Sciences on November 8.

THE FitzPatrick lectures of the Royal College of Physicians, London, on "The history of anatomy" were given by Dr. Charles Singer on November 11 and 13.

THE Schorstein memorial lecture was delivered by Sir Arthur Keith in the anatomical theater of the London Hospital Medical College on December 17 on the subject of the clinical importance of the bulbus cordis.

THE Huxley memorial lecture of the Royal Anthropological Institute was delivered on November 25 in the rooms of the Royal Society, London, by Professor Réné Verneau on the subject "La race de Neanderthal et la race de Grimaldi: leur rôle dans l'humanité."

ON October 18, Sir Archibald Garrod delivered the Harveian oration before the Royal College of Physicians. His subject was "The debt of science to medicine."

THE three hundredth anniversary of the birth of Thomas Sydenham was commemorated at a meeting of the president and fellows of the Royal College of Physicians of London on November 12. There was a reception in the evening, followed by an address by the president, Sir Humphry Rolleston.

DR. GEORGE CHANDLER WHIPPLE, professor of sanitary engineering at Harvard University, died on November 27, aged fifty-eight years.

DR. EDMOND SAUCHON, formerly professor of anatomy and of clinical surgery at Tulane University, recently died at the age of eighty-three years.

DR. WALTER ELMORE FERNALD, for more than thirty-five years superintendent of the Massachusetts School for Feeble-minded, died on November 28, aged sixty-five years.

SIR MAURICE FITZMAURICE, F.R.S., distinguished English engineer, died on October 18, aged sixty-three years.

R. W. M. THOMSON, assistant lecturer in chemistry at King's College, University of London, died on November 5, aged twenty-five years.

DR. B. GLANVILL CORNEY, English physician and anthropologist, known for his work with the Fijians, died on September 29, at the age of seventy-three years.

THE American Ornithologists' Union at its forty-second annual meeting held recently in Pittsburgh reelected the present staff of officers to serve for the coming year. The list follows: *President,* Jonathan Dwight, New York City; *vice-presidents,* Joseph Grinnell, Berkeley, Calif.; Alexander Wetmore, Washington, D. C.; *secretary,* T. S. Palmer, Washington, D. C.; *treasurer,* W. L. McAtee, Washington, D. C.

THE nine hundred and ninth meeting of the Philosophical Society of Washington was held in the Cosmos Club auditorium on November 29, when Dr. W. W. Coblentz gave an illustrated lecture on "The measurement of planetary temperatures" and W. D. Collins talked on the "Temperature of air and water."

THE Association of Scientific Apparatus Makers of the United States met on November 14 and 15, at the plant of the Taylor Instrument Companies, Rochester, N. Y. After a luncheon, a trip through the plant and an informal "get together," papers were read, followed by discussions.

ON November 15 the Royal Canadian Institute celebrated its seventy-fifth anniversary. Addresses were delivered by Sir Robert Falconer, president of the University of Toronto, on "The humanism of science," and by Dr. A. P. Coleman, professor of geology in the University of Toronto, on "The Royal Canadian Institute's contribution to science."

IN connection with the forthcoming meeting of the American Association for the Advancement of Science in Washington, extensive plans have been made for the sessions of Section E, Geology and Geography, through Dr. Mendenhall, chief geologist of the Geological Survey, and vice-president and local representative of the section, rooms for the sessions have been secured in the survey building. This will add much to the interest of the meeting particularly for the geologists attending. In order that some geologists may attend the meetings of both the association and the Geological Society of America, at Ithaca, it has been decided to begin the sessions of the section at 10.00 A. M. on Tuesday, December 30, and continue them to January 2. On the evening of December 30, an informal dinner will be held by the members of Section C and the Association of American Geographers, at the Blue Triangle Center and Recreation Club of the Y. W. C. A. at 7.00 P. M., the price per plate being $2.00. During the evening the addresses of the retiring president of the Associa-

tion of American Geographers and of the retiring vice-president of Section E, will be given, and the remainder of the evening will be spent in a social gathering so that the members may become better acquainted. It is intended to devote one session to a symposium on "Ancient climates" and several afternoons to excursions to the Geophysical Laboratory, the museums, and, if weather conditions are favorable, the field in the vicinity of Washington. One session will be devoted to the problems which the geological and geographical division of the National Research Council is working on.

The Journal of the American Medical Association states that the Fonds d'Etudes Roche has been organized by the manufacturing chemists, F. Hoffmann-La Roche and Co., who offer space in their establishment, at Basel, to research workers in experimental medicine and biology, and all facilities for research and a stipend, if desired. Only exceptionally will a longer course than three months be granted. The places are open to medical students, physicians and other scientists. Professor F. de Quervain, Kirchenfeldstrasse 60, Berne, is chairman of the committee, to whom application must be made and credentials presented. The work is entirely independent of regular work in the establishment, and the subject must be approved by the committee, consisting of Professors Cloetta, Zurich; Michaud, Lausanne; Roch, Geneva; Staehelin, Basel, and de Quervain, Berne.

UNIVERSITY AND EDUCATIONAL NOTES

A GIFT of $250,000 has been made to the Hampton and Tuskegee Endowment Fund by an anonymous New York banker.

A CONTRIBUTION of £1,000 has been received from Lord Glendyne towards the Jubilee Endowment Fund of the London School of Medicine for Women, which is intended to provide for the endowment of three chairs in the school—anatomy, physiology and pathology. The sum of £27,500 has now been raised towards the completion of the proposed £60,000 endowment.

DR. W. J. MILLER, for some years professor of geology in Smith College, has accepted a position as professor of geology and chairman of the department in the University of California, Southern Branch, Los Angeles.

WARREN E. LORING, of the University of Maine, has been appointed assistant professor of mathematics at Colby College, to fill the vacancy caused by the illness of Professor Benjamin Edward Carter.

DR. GEO. F. WEIDA, of Kenyon College, has been appointed professor of chemistry at Centre College, Kentucky.

AT the Polytechnic Institute, of Brooklyn, N. Y., Dr. Parke B. Fraim, of Lehigh University, has been appointed assistant professor of physics, and Frank D. Carvin, of the University of Pennsylvania, assistant professor of mechanical engineering.

AT Tulane University, Dr. Parry Borgstrom has been appointed assistant professor of industrial chemistry, and A. Lee Dunlap, assistant professor in mechanical engineering, in the place of Ivor O. Mall, who has resigned.

DR. WALTER C. CRAIG, assistant director at the Johns Hopkins Hospital, Baltimore, has resigned to accept a position in the department of surgery at Yale University School of Medicine. Dr. Craig will be succeeded by Dr. John H. Snoke, who until recently was superintendent of St. Luke's Hospital, Shanghai, China.

MRS. LUGAN KEENE has been appointed professor of anatomy at the London School of Medicine for Women.

SIR CUTHBERT WALLACE has been elected dean of the faculty of medicine at the University of London.

PROFESSOR H. H. DIXON, whose appointment to the Regius chair of botany in the University of Glasgow was recently announced, is unable to accept the appointment.

DISCUSSION AND CORRESPONDENCE

A NEW FORMULA FOR THE ELECTRICAL RESISTANCE OF CERTAIN INHOMOGENEOUS SYSTEMS

IN a recent issue of SCIENCE (1924, lix, 403) Dr. F. H. MacDougall proposes a formula for the resistance of living cells suspended in a medium.

$$R = M\left[\frac{1 + a\left(\frac{S - M}{2S + M}\right)}{1 - 2a\left(\frac{S - M}{2S + M}\right)}\right]$$

In which S is the resistance of the cells, M the resistance of the medium and R the resistance of the suspension of cells in the medium and a the cell volume. This formula is the same as formula 17, page 440, in Clerk Maxwell's "Electricity and Magnetism," third edition, Vol. 1, 1892, provided the algebra is translated into the same form. Maxwell's formula is:

$$R = M\left[\frac{(2S + M) + a\,(S - M)}{(2S + M) - 2a\,(S - M)}\right]$$

By dividing both numerator and denominator of the fraction inside the brackets by $(2S + M)$ we obtain MacDougall's formula.

In a paper by F. H. MacDougall and R. G. Green in the *Journal of Infectious Diseases* (1924, xxxiv, 195), the formula for the resistance is:

$$\frac{1}{R} = \frac{1-a}{M} + \frac{a}{S}$$

after translating one term into the conventions of MacDougall's paper. In a paper by Karl Lichtenecker on the resistance of certain composite conductors in the *Physikalische Zeitschrift,* 1918, xvii, 381, is given a formula which when translated into MacDougall's terms is:

$$R = \frac{SM}{(1-a)\,S + aM}$$

If we reduce MacDougall's equation to a common denominator we obtain

$$\frac{1}{R} = \frac{(1-a)\,S + aM}{SM}$$

and by taking the reciprocals of each side of this equation we obtain the equation used by Lichtenecker.

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HOW MANY FIGURES ARE SIGNIFICANT?

THE readers of SCIENCE are aware that varying practices are followed by the workers in the natural and social sciences regarding the number of decimal places kept and reported in their investigations. A definite and uniform practice would conduce to general understanding. Discussions with my colleagues regarding certain quantitative studies of my own which promised to be serious and worth-while have become mired around the decimal point. As a result of this I have determined upon a rule for my personal guidance which I believe may be of general utility.

Determine the probable error of the measure involved, by statistical means if possible, otherwise estimate it. *Keep to the place indicated by the first figure of ½ the probable error.*

As an illustration, suppose we calculate the mean and standard deviation of a certain series and find:

Mean = 81.7433
Standard deviation = 12.8294
Population = 100
The probable error of the mean according to the usual formula = .865
The probable error of the standard deviation according to the usual formula = .612
½ the probable error of the mean = .432
½ the probable error of the standard deviation = .306

Following the rule, we would publish: Mean = 81.7 and the standard deviation = 12.8.

As a second illustration: Suppose we have a correlation coefficient of .75248 from a population of 400. Its probable error, according to the usual formula, is .0146. One half the probable error equals .0073. Accordingly, the correlation coefficient should be published as equal of .752.

The argument underlying this rule is that one should not throw away data that are likely to influence judgment. A difference of 1 probable error indicates that the chances are 3 to 1 that the difference is of the sign indicated. This is scant evidence of significance but not entirely meaningless. A difference of one half of the probable error indicates that the chances are about 5 to 3 that the difference is of the sign indicated. For ordinary purposes this is of insignificant moment. Failure to keep more figures introduces a slight error, but keeping them introduces a much greater error in interpretation by suggesting an accuracy which does not exist. It is necessary to strike a balance and the rule suggested is offered as a reasonable compromise.

It is intended that it be applied to raw or original measures or observations as well as to derived constants such as averages, measures of variability, etc. It is to be expected that computation work preceding publication will be carried to at least one figure further than the final published result.

TRUMAN L. KELLEY
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OPPORTUNITIES FOR SCIENCE TEACHERS IN NEW YORK HIGH SCHOOLS

A LETTER requesting information regarding opportunities for science teachers in the high schools of New York City was received by the writer some months ago from an associate professor in a large collegiate institution east of the Mississippi. The information furnished may be of interest to others and is outlined below. There is a real opportunity for important work, both in science education and in supplementary graduate work in science.

(1) There has been for some years a shortage of well-qualified teachers, especially of men for the boys' high schools. Three successive examinations in biology netted not more than three or four successful candidates, who were immediately appointed.

(2) The population of the New York City high schools stands at present at one hundred and ten thousand, and increases by thousands every year. All these ought to have several courses in science, and it appears that recognition of this fact is growing on the part of the administrative officials, and science work is entering a floodtide. At present between four and five hundred specially selected science teachers are required to offer the courses now given.

(3) The salary of the regular high school teacher,

called "assistant teacher," ranges from nineteen hundred to thirty-seven hundred dollars. Credit is given in the initial salary for recognized outside teaching experience and graduate work. By a further examination for the license of "first assistant," a progression to forty-two hundred dollars is possible, with administrative duties as chairman of department. Such departments range in size from two or three to forty teachers. High schools range from one to eight thousand pupils. At the last count there were thirty-five secondary schools ranked as high schools, with more new ones in prospect.

(4) Opportunities for continued graduate work and research are probably not equalled or even approached elsewhere in the country. The educational problems constitute an intensely interesting and important field of work in themselves, and New York is headquarters for more kinds of pure and applied scientific research than anywhere else. The universities, professional schools, libraries, science foundations, botanic gardens, museums, industrial establishments, et al., all offer problems by the score, with facilities for the qualified investigator. For those who have not finished graduate study toward a degree, the universities offer important graduate courses on Saturdays.

(5) Full details regarding the stated examinations, etc., may be obtained by addressing the Board of Examiners, 500 Park Ave., New York City. Following are paragraphs taken from their circular of information, and giving some of the facts a prospective candidate for the examination would be interested to know.

(a) Teaching positions in New York City are secured by competitive examination, a part of which is written. These examinations usually held twice a year, in November or December, and in March or April, usually at a time when the New York City public schools are not in session.

College graduation and one year's teaching experience, or, in lieu of teaching experience, one year of postgraduate work which must include 60 hours in the methods of teaching the subject.

(b) It takes nearly a year for examiners to make proper evaluation of the candidates' references, scholarship and records of service so that persons applying for New York City positions who take the examination should not look for appointment any earlier than one year from the date of the written examination.

Copies of the last written examination question paper may be obtained, while they last, from the Board of Examiners, 500 Park Avenue, New York, upon request, enclosing a stamped and self-addressed envelope.

RALPH C. BENEDICT

STUYVESANT HIGH SCHOOL AND
BROOKLYN BOTANIC GARDEN

SUGGESTED MODIFICATIONS OF THE CELLOIDIN METHOD

UNDER the caption "A shorter celloidin method" there recently appeared in SCIENCE (No. 1542, July 18, 1924, p. 67) a description, signed by J. E. Lodewick, of a tank made of an iron pipe, for use in imbedding tissues with celloidin under pressure. The present writer wishes to suggest some modifications which have been found advantageous.

Instead of using a piece of iron pipe for the tank a heavy glass jar can be used, provided the pressure is not run too high. In an apparatus of this kind, described in detail by the writer in the April, 1914, issue of the Proceedings of the Society of American Foresters, a pressure of 30 pounds per square inch can safely be used.

The great advantage of the glass jar is, of course, that the material can be observed without opening the chamber. Hence, certain obvious precautions can be taken against too rapid release of pressure and attendant bubbling over of the celloidin or the celloidin becoming too low on account of an insufficient original supply.

The writer has also found that woody material can be satisfactorily imbedded by the pressure method by using only a 10 per cent. solution of celloidin, provided a liberal supply is used to begin with. Thus, one avoids the necessity of any transfer of material to a higher concentration. Another way of hastening the process with tissues that can endure higher temperatures is to heat and cool the chamber alternately at intervals of several hours. The increased pressure should be applied particularly while the celloidin is cooling, so as to secure penetration into the cell cavities while the gases are contracting and condensing within.

ARTHUR KOEHLER

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A CURIOUS SURGICAL CASE

I HAVE received from Mr. Nisuke Takahasi, a teacher in a high school in Kumamoto, Japan, a specimen of a fish somewhat noted in Japanese surgery.

It is a fish two and four fifth inches (7.0 cm) long taken from a man's throat, in which it had become lodged. The specimen concerned is a common fresh water fish of the clear streams of Southern Japan, locally known as Oyarami or Kawamebaru, very closely related in fact as well as in appearance to some of our American freshwater sun-fishes (*Centrarchidae*). Its scientific name is *Bryttosus kawamebari* (Schlegel).

The specimen is virtually perfect, although apparently somewhat emaciated. How it was swallowed is not explained, but it is evident that its sharp dorsal spines would hold it in place once swallowed. The specimen was presented to Stanford University by Dr. Toyoji Nishiyama, of the Municipal Hospital at Kuverme, at the suggestion of Dr. Chiyomatsu Ishikawa, of the Imperial University of Tokyo.

DAVID STARR JORDAN

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SCIENTIFIC BOOKS

Human Origins, a Manual of Prehistory. By GEORGE GRANT MACCURDY, *Ph.D.* Vol. I, *The Old Stone Age and the Dawn of Man and his Arts,* 440 pages; Vol. II, *The New Stone Age and the Ages of Bronze and Iron,* 516 pages. D. Appleton and Company, New York.

A READER whose interest in the prehistoric archeology and ethnology of Europe is professional will scrutinize the qualifications of the author of any work on this subject before turning over the pages of the work itself. Such a reader will desire to know whether or not the author has a first-hand knowledge of his subject. What experience has he had in the excavation of archeological sites? Does he know the collections of prehistoric material in European museums? Is he competent to pronounce upon geological and paleontological questions? Is he a physical anthropologist? Unless he is satisfied with the qualifications of the author, the worker in the field of knowledge dealt with will decline to give serious consideration to his writings.

In the present instance the reader may proceed to the perusal of "Human Origins" with complete confidence that it is the output of a competent scientist writing within the field of his own special knowledge and experience. Dr. MacCurdy has been trained in the methods of European prehistoric archeology and in the technique of physical anthropology by the foremost Continental authorities in these subjects. For many years he himself has conducted excavations in prehistoric European sites; his writings have furnished American anthropologists with the latest information on progress of the science in Europe; he is one of the two or three Americans who are recognized abroad as authorities on European prehistoric archeology. Further, he brings to bear upon European questions his extensive experience in the archeology and physical anthropology of the New World.

To a teacher of European prehistory the outstanding merit of Dr. MacCurdy's work is its comprehensiveness. It deals with the entire prehistoric period. It does not leave the reader stranded on a terminal moraine in the company of fossil men, extinct animals and chipped stone implements. With the exception of Déchelette's great work ("Manuel d'archéologie préhistorique, Celtique et Gallo-Romaine"), now somewhat out-of-date, "Human Origins" is the one satisfactory attempt to carry the prehistory of man in Europe through to the present era in an adequately detailed treatment.

The first volume deals with the Old Stone Age and fossil man. Here Dr. MacCurdy is at his best. Climatic and geographical conditions, prehistoric chronology, types of fossil men and animals, industries and arts of the various archeological periods—all these subjects are thoroughly discussed, but with due regard for their relative importance. A disproportionate amount of space is not allotted to any particular feature. MacCurdy does not build his book upon some one aspect of prehistory, subordinating all other subjects to that of his own specialized knowledge and interest. A few crucial points in this volume should be noted. The author accepts the Foxhall eoliths of the Pliocene period; he assigns the Acheulian industry to the Rissian glaciation and places the beginning of the Mousterian industry in the third interglacial (Riss-Würm) period; he regards the Piltdown mandible as human, but is not certain that it belongs with the associated brain-case fragments. The section on fossil man is concise but complete. In the opinion of the reviewer, Dr. MacCurdy does not sufficiently consider the evidence pointing toward the existence of an essentially modern type of man in the Lower Paleolithic Age.

The second volume is devoted to the Mesolithic, Neolithic, Iron and Bronze Ages and to valuable appendices dealing with the stratigraphy of paleolithic sites and with the distribution of paleolithic art and of prehistoric monuments. Appreciation of the inclusion in this work of a summary of the early metal periods has already been expressed. What the author has to say of the Bronze and Iron Ages is, so far as it goes, excellent. But of the 918 pages of text, plates and bibliography included in the two volumes, only 52 pages are devoted to the Bronze Age, and the Iron Ages are crowded into 71 pages. Yet from the historical, ethnological or archeological viewpoints these are the most important periods of European prehistory. Fossil man is accorded 136 pages of discussion and recent man receives a scant 7 pages. There is no adequate treatment of late prehistoric and proto-historic racial movements. The reviewer does not cavil at the thorough and detailed treatment of the Paleolithic Age to which Dr. MacCurdy has devoted the bulk of his work. He only regrets that the author did not extend his treatise sufficiently to satisfy also the acute academic need

for a full discussion of the later periods. Civilization, after all, is cumulative and the nearer the archeologist approaches to the historical period the more extensive his material becomes and the more numerous and vital are the problems which he must endeavor to solve.

"Human Origins" is the most useful manual of prehistory available to readers of English. It surpasses the work of Déchelette in its superior grasp of problems of physical anthropology. The illustrations of MacCurdy's work are also more numerous and better. The classical French work is, however, better balanced. The scant notice accorded to the archeology of the Eastern Mediterranean area is less excusable in a general manual of prehistory than in a work primarily concerned with the archeology of France. But, without a doubt, students of prehistory are to be congratulated upon the publication of this scholarly treatise which is the work of no amateur but of a dependable authority.

E. A. HOOTON

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SPECIAL ARTICLES

ELECTRIC TRANSPORT OF FLUID ACROSS MAMMALIAN SEROUS MEMBRANES

EXPERIMENTS performed during the past year have shown that the serosae of mammals are amphoteric membranes. If the membrane is bathed in dilute blood or buffer more alkaline than a certain critical hydrogen-ion concentration and traversed by an electric current, the liquid streams through the membrane toward the cathode. With buffers more acid than the reversal point, streaming is toward the anode. A reversal in sign of the electrokinetic potential difference[1] between the membrane pore walls and the liquid in the pores is thus indicated.

The mesenteries of anesthetized living dogs, cats and rabbits, the mesenteries and parietal pericardia and pleurae of the same species, post-mortem, and two human pericardia, post-mortem, have thus far been tested. These membranes are essentially sheets of connective tissue, bearing blood vessels, lymphatics and nerves, and in some instances, fat cells, lined on each surface by a single layer of pavement mesothelial cells. Intercellular fibers form the major bulk of the lean membranes; these are predominantly collagenous except in the pleural sheet between pericardium and diaphragm where elastin fibers may be present in large proportion.

The reversal point of a complex, amphoteric membrane may be defined as that concentration of H-ions in a given solution within the pores of the membrane, traversed by an electric current, at which the total electroendosmotic current through the membrane is zero.

The mean values of the reversal points with citrate-phosphate buffers for all tissues studied have been between pH = 4.3 and pH = 5.3. By using buffers alternately more acid or alkaline than the reversal point the direction of liquid flow across any given membrane site may be reversed an indefinite number of times. The time interval required is only that taken for the requisite manipulation in changing buffers and making the runs.

The buffers used have been dilutions of McIlvaine's[2] citric acid-sodium phosphate mixture and certain isotonic, physiologically balanced buffers. The latter were citrate-phosphate mixtures containing Na, K and Ca in the proportion of Ringer's solution, and made isotonic by the addition of glucose or of glycerin. The glycerin buffer was found preferable.

The mean values of the reversal points for the several membranes when bathed in the hyptonic unbalanced buffer and in the isotonic, physiologically balanced buffers showed only small and inconstant differences.

The fat and lean membranes in each category similarly showed small if any difference in the positions of the mean reversal points.

The apparent reversal points for the mesenteries of living animals proved to be lower than those for the mesenteries post-mortem. This low value in the animals with functioning circulation has been interpreted as essentially due to admixture with the buffers of buffer salts from the blood. Distinct differences have not been detected between the reversal points of the membranes in the first compared with later hours or days post-mortem, with the possible exception of a small shift toward the acid range of the fat pericardia reversal points when tested several days post-mortem.

The approximate mean reversal points found with the citrate-phosphate buffers were as follows: for mesenteries of living animals, pH = 4.4; for pleurae, post-mortem, pH = 4.6; for mesenteries, post-mortem, pH = 4.8; for lean and fat pericardia, post-mortem, pH = 5.1. The mean reversal point estimated for the human pericardia was about pH = 5.0. The concentration of hydrogen-ions requisite for reversal of the membranes with these buffers containing polyvalent anions is greater than with an acetate buffer.

The ready reversibility of the membranes would seem to indicate that their charging, *i.e.*, electrokinetic p. d., is ultimately dependent largely upon the dis-

[1] Freundlich, H., and Gyemant, A., *Ztschr. f. physik. Chem.*, 1922, c, 182.

[2] McIlvaine, T. C., *J. Biol. Chem.*, 1921, xlix, 183.

sociation state of certain amphoteric components of the membranes. The position and sharpness of the reversal points is strongly suggestive of these ampholytes being proteins. The conclusion seems warranted that proteins probably constitute an important part at least of the material of which the membrane cell surfaces are composed.

STUART MUDD

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SELACHIAN "DENTICLES" IN THE CAT[1]

IT is now well known that the human lips at birth possess an inner zone beset with "long, soft, villus-like outgrowths." In a few weeks, these villi largely disappear, though the zone itself remains more or less distinctly marked throughout life. Denuded of their epithelium, Ruysch figured them as "papillae," in 1707. Luschka (1863) was the first to describe them with modern precision, and since then they have been the subject of important studies by Neustätter, Stieda, Ramm and others. The portion of the lip which bears the villi is clearly distinguishable to the naked eye, and the individual projections, with their vascular cores, may be seen on low magnification. Neustätter, in 1895, remarked that so far as his investigations showed, human lips alone are provided with this double zone—the outer of which is smooth, and the inner, villous—and he rather fantastically ascribed the condition to the shortness of the nipples and flatness of the central area of the breasts in women. Thus human infants require a special "Greifapparat" for an airtight contact!

Rejecting this interpretation—of "non-skid" lips, as his assistant called them—and after reviewing the literature in the way here outlined, Dr. F. T. Lewis proposed a different interpretation (Buffalo meeting of the American Association of Anatomists, April 16, 1924). He showed photographs of the labial "villi" in man, and others of the teeth of the skate, both intact and in sections, and proposed to regard them as homologous structures. That is to say, he considered the human labial villi, notwithstanding their small size, their tendency to point outward and their lack of dentine, as actual denticles or potential selachian teeth. In the human oral region, then, in addition to the gill clefts, there would be another striking suggestion of the ichthyoid plan of development.

The present account is intended to report the finding of bilaterally arranged papilliform structures on the inner surface of the upper lip in the newborn kitten. These are very clearly the equivalents of the villi or denticles of the human lip, though the inner zone which they form is not exposed at the oral margin; they are wholly within the lips.

On the upper lip of the kitten they are arranged in three groups in the specimens studied—a median group, and on either side, a lateral group.

The median group consists of a single row of four large incisor-like papillae, which might possibly be mistaken for teeth, but the well-defined dental ridge is further within the mouth, and these papillae have no connection with it. Of these four papillae those next the midline are the largest and measure 1.0 mm in height by 0.75 mm in width at the base. They are flattened in the same plane as the human incisors. Their free margins are somewhat rounded and are without serrations. The lateral members of this group are very similar though a little smaller.

On either side of the median group is a lateral group of from twenty to thirty smaller papillae, bluntly conical in shape and arranged in poorly defined rows. Those in one row may partially overlap the units in the next row. These papillae do not stand erect, but their tips are turned somewhat forward and toward the median line. Beyond the lateral groups, in the direction of the corners of the mouth, a portion of the lip is quite smooth.

The papillae in all the groups consist of connective tissue cores covered with a very thick epithelium, much thicker than the epidermis. In these respects they are like the papillae of the human lips, but they are neither so slender nor so vascular. No dentine has been observed.

The location of the villi would seem to preclude the possibility of their serving to strengthen the animal's grasp upon the nipple. Without assigning to these rather remarkable structures any function, I would regard them, provisionally at least, as "denticles," for superficially their resemblance to selachian teeth is very striking.

During the month that this report has been in press, 130 kittens and cats have been examined, and although the villi early disappear in man, in the cat they are found to be retained throughout life. Their number diminishes, and those of the median group become merely moundlike masses limited by furrows. In the lateral groups, however, the loss in number is accompanied by an increase in size, and the acquisition of a more definitely pointed character, in those which remain. They may attain a length of 2.75 mm. and a breadth of 1.25 mm. In general they point downward and outward, but instances are not rare in

[1] A study conducted as Medical Fellow of the National Research Council.

which they project upward or even directly backward into the oral cavity. The further study of these remarkable "denticles" is in progress.

BARRY J. ANSON

HARVARD MEDICAL SCHOOL,
SEPTEMBER, 20, 1924

THE AMERICAN CHEMICAL SOCIETY

DIVISION OF BIOLOGICAL CHEMISTRY

R. A. Dutcher, *secretary*
W. T. Bovie, *chairman*

A Study of the Nutritive Value of Gelatin: THOMAS B. DOWNEY. The results of an investigation of the supplementary value of gelatin as a protein where fed with a number of foods common to the dietary, and of the influence of the colloidal properties of gelatin upon the digestion and absorption of various dairy products. Feeding tests with the albino rat have shown that gelatin, as a protein, supplements the protein deficiency of wheat, wheat products, oats, rye, barley and barley products. Gelatin does not, however, increase the food value of navy beans or corn. Further observations have demonstrated that gelatin by virtue of its colloidal properties increases the nutritive value of dairy products, such as cow's whole milk, egg and milk, and ice cream (typical commercial formulas).

The Antirachitic Action of Fresh Cod Liver Oil as Compared with that of a Concentrate Prepared from the Oil: HARRY E. DUBIN. Young rats were placed on a rickets-producing diet for a period of 30 days. During this time, one group of rats received daily doses of varying quantities of fresh cod liver oil. Another group was given an equivalent amount of cod liver oil in the form of a concentrate prepared from the oil. A third group acted as controls. At the end of the experimental period, the animals were X-rayed. The controls showed rickets, while those receiving either cod liver or the concentrate remained free from rickets.

The Physiological Activity of Some Synthetic Compounds Closely Related to Thyroxin: E. C. KENDALL and A. E. OSTERBERG. Alpha oxy-indol propionic acid in glacial acetic acid will substitute bromine on its imino group and HBr will then split out between the N and No. 7 carbon. This bond also occurs in all the halogen substituted derivatives of alpha oxy-indol propionic acid. Experiments have demonstrated the great physiological activity of this bond which under the conditions in the animal organism acts as an active hydrogen acceptor. The relation of this finding to thyroxin and oxidation in the animal organism will be discussed.

A New Type of Organic Phosphoric Acid Compound Isolated from Blood: ISIDOR GREENWALD. A compound which appears to consist of two molecules of phosphoric acid united with one molecule of 1-glyceric acid has been isolated from pig blood, in which it forms at least one third of the total "acid-soluble" phosphorus. It is very resistant to acid hydrolysis. A compound of the same nature is present in the blood of man and the dog but not in that of the cow and the sheep.

Quantitative Determination of Vitamin A: H. C. SHERMAN and H. E. MUNSELL. In order to determine the relative amounts of vitamin A in foods, a method has been developed upon the plan proposed by Drummond, Coward, Zilva and their coworkers. Standardized animals are fed a vitamin-A-free, otherwise adequate diet until growth ceases; and then the amount of food which when fed daily will just suffice to permit a gain in weight of approximately 3 grams per week for 8 weeks is ascertained. Standardization of animals, diets, procedure and interpretation is discussed.

Further Experiments upon Vitamin A: H. C. SHERMAN and L. B. STORMS. This investigation deals with (1) the age at which experimental animals (albino rats) attain their maximum body store of vitamin A, (2) the influence of previous feeding upon the relative store of vitamin A in the body at a given age, (3) the influence of variations in body weight at a standard initial age, (4) the influence of family, and (5) the question whether the sexes differ in their capacity to store vitamin A or to endure deprivation of this vitamin.

A Ration Low in Calcium as a Factor in the Production of "Stiffness" in Swine: L. A. MAYNARD, S. A. GOLDBERG and R. C. MILLER. The trouble in pigs variously referred to in popular language as stiffness, paralysis and rickets was produced on a ration low in calcium, consisting of yellow corn, wheat middlings and oil meal, but did not result where the same feeds were supplemented with bone meal and limestone, nor was it produced on a ration of yellow corn, middlings and fish meal. The femurs of the pigs receiving the low calcium ration contained less than two thirds as much calcium and phosphorus as the femurs of littermates on the other two rations. Corresponding differences were found in the structure of the bones on section. On microscopic examination the bones from the pigs on the ration low in calcium showed marked and constant lesions. The data indicate that the stiffness was a result of inadequate mineral nutrition of the bones due to a ration deficient in calcium.

Vitamin B in Evaporated Milks Made by Vacuum and Aeration Methods: R. ADAMS DUTCHER, EMMA FRANCIS and W. B. COMBS. Sterilized and unsterilized evaporated milks, made by vacuum and aeration methods, were fed to rats receiving a ration deficient in Vitamin B. Control groups were fed equivalent amounts of raw herd milk from which the evaporated milks were made. The results indicate that evaporation (by vacuum and aeration methods) did not injure Vitamin B appreciably, although slight destruction took place. After sterilization of the evaporated milks, the destructive effect was more marked, particularly in the evaporated milks made by the aeration method. The destructive effect can hardly be considered of serious nutritive significance.